REMARKS

Claims 24-39 are rejected. Claims 1-23 and 40 are withdrawn from consideration. Claims 24, 31, and 32 have been amended. Claims 1-40 are presently pending in the application. Favorable reconsideration of the application in view of the following remarks is respectfully requested.

Claim Objections:

The Examiner has objected to Claim 24 because of the limitation "loaded" recited in line 5 of the claim. Claim 5 has been amended accordingly.

The Examiner has objected to Claim 31 because of the l "surfaces" recited in line 2 and "particles" recited in line 3 should be in the singular forms. Claim 31 has been amended accordingly.

The Examiner has objected to Claim 32 because the limitation "surfaces" recited in line 3 should be in the singular form. Claim 32 has been amended accordingly.

Rejection Of Claims 24-39 Under 35 U.S.C. §103(a):

The Examiner has rejected Claims 24-39 under 35 U.S.C. §103(a) as being unpatentable over Rembaum et al. (US 4,929,400) in view of Mihara et al. (US 4,331,444) and de Jaeger et al. (US 4,837,168), as Rembaum et al. disclose polymeric microspheres adapted to be used for immunoassays and a method for producing them, the microspheres are acrylic and can range from 1000 Angstroms to 100 microns in size, each microsphere comprises functional groups capable of binding proteins and a dye for visually detecting the microspheres, however, the reference does not disclose that the dye comprises a photographic coupler. The Examiner indicates that De Jaeger et al. disclose latex label adapted to be used for immunoassays, the latex particles are coupled to dye-forming couplers that can be developed to form cyan, magenta or yellow dyes, the dyes are used to visually detect the occurrence of a reaction of interest, phenol or a naphthol type compounds produce cyan dyes, pyrazolone type compounds form magenta dyes and open chain ketomethylene type compounds form yellow dyes and Mihara et al. disclose a method for immunoassay using a phenol or a naphthol coupler, a pyrazolone coupler, and an open chain ketomethylene coupler that are developed by oxidizing developing agents to form cyan, magenta or yellow dyes, respectively, and the couplers are dissolved in high boiling solvents before the solution is applied to the target substrate or support, making it obvious to one of

ordinary skill in the art to dye the microspheres disclosed by Rembaum et al. with the dye-forming couplers dissolved in high boiling solvents disclosed by Mihara et al. and de Jaeger et al. since the 3 dye colors provide versatility and diversity in detection.

Rembaum discloses a process for the production of polymeric particles and, more particularly, evenly-sized, magnetic or non-magnetic, microspheres by the polymerization of falling or suspended uniformly- sized and shaped droplets in a containerless environment. The polymeric microspheres with very precise size and a wide variation in monomer type and properties are produced by deploying a precisely formed liquid monomer droplet, suitably an acrylic compound such as hydroxyethyl methacrylate into a containerless environment. The droplet which assumes a spheroid shape is subjected to polymerizing radiation such as ultraviolet or gamma radiation as it travels through the environment. Rembaum fails to disclose a microsphere loaded with both a photographic coupler and a high boiling organic solvent.

Mihara et al. discloses a method photochemically analyzing in a quantitative manner trace components utilizing immune reaction by marking or labeling an antigen or antibody with a marker. An immune reaction is caused using an antigen or antibody marked with a fogging agent for silver halide, the labeled antigen or antibody is separated from the labeled antigen-antibody reaction product, the silver halide is developed in the presence of either one of the labeled antigen or antibody and the labeled antigen-antibody reaction product, and the density obtained is measured. The method is comparable to radioimmunoassay in having high reproductibility and sufficient sensitivity but does not involve any risk due to radiation. In Mihara, the coupler is dissolved into a high boiling organic solvent and dispersed in a gelatin binder along with silver halide particles, to provide a silver halide particle tagged with a fogging agent/biological probe complex and coupler, all dispersed in a gelatin binder. The coupler is not truely in intimate contact or loaded in a microsphere. The amount of coupler that gets developed into dye depends on the amount of silver halide particles that are fogged by the complex of the antigen and fogging agent that is attached to the silver halide particles. The color forms as a dye cloud around the silver halide particles as development occurs. No individual particles are detected and you simply read out color density as a function of the amount of silver

development. Mihara fails to disclose a microsphere loaded with both a coupler and a high boiling solvent.

DeJaeger et al. relates to a method for the detection of specific binding agents and their corresponding bindable substances by employing a label which is a latex particle which can be visually detected. DeJaeger fails to disclose a microsphere loaded with both a coupler and a high boiling solvent.

The present invention relates to a polymeric particle for use in a microarray comprising polymeric particle, loaded with at least one photographic coupler and high boiling solvent, and having at least one functionally active group that can interact with a biological probe. In the case of the polymer particles of the present invention, the developer penetrates the microsphere to reach the loaded coupler and the developed coupler, still loaded in the microsphere, produces a colored microsphere. These particles are readily observable in a microscope after they develop color.

To establish a prima facia case of obviousness requires, first, there must be some suggestion or motivation, either in the references themselves, or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art references (or references when combines) must teach or suggest all the claim limitations. The level of skill in the art cannot be relied upon to provide the suggestion to combine references. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in the applicant's disclosure. *In re Rouffet*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998).

The present invention relates to a microsphere loaded with both a photographic coupler and a high boiling solvent. Rembaum discloses polymer microspheres, but fails to disclose microsphere which are loaded, that is, imbibed with, photographic coupler and high boiling solvent. Mihara, which teaches the use of photographic couplers in silver-halide emulsion layers (col. 10, lines 3-4) and the use of high and low boiling solvents (see col. 10, lines 6-7, plus lines 14-15) to introduce the couplers into the gelatin layer, fails to mention the use of a microsphere containing photographic coupler or both photographic coupler and high boiling solvent. DeJaeger teaches microspheres containing photographic

coupler, but fails to teach microspheres containing both high boiling solvent and photographic coupler. None of the references discloses a polymeric particle containing a photographic coupler and a high boiling solvent. At best, a combination of the references would produce a microsphere containing coupler and that coupler is soluble in high and low boiling organic solvents.

Neither is there any likelihood of success. The Examiner indicates that it would have been obvious to one of ordinary skill in the art to dye the microspheres disclosed by Rembaum et al. with the dye-forming couplers dissolved in high boiling solvents disclosed by Mihara et al. and de Jaeger et al. since the 3 dye colors provide versatility and diversity in detection. However, none of the references teach a microsphere containing, specifically, high boiling solvent, and therefore produce no likelihood of success in producing a microsphere containing high boiling solvent. The present specification indicates that "Particles in the sub-micronic range (nominally less than 100 nanometers) are difficult to detect by optical means. In addition, a polymeric bead solvated with a color forming moiety is difficult to develop into color using chemical means." The examples of the present specification indicate that the presence of the high boiling solvent in the microsphere enhances the intensity of the developed color by maximizing developed dye density (pg. 13, lines 21-25), resulting in enhanced penetration of developer into the microsphere, making the small particles easier to detect and individually identify than microspheres containing coupler alone. See Table I, pg. 24. It is the solubility of the developer in the high boiling solvent that results in enhanced color development, not the solubility of the loaded coupler in the high boiling solvent. The cited prior art is silent with regard to the solubility of developer in high boiling solvent, resulting in enhanced color development of coupler loaded in a microsphere in which high boiling solvent is also loaded.

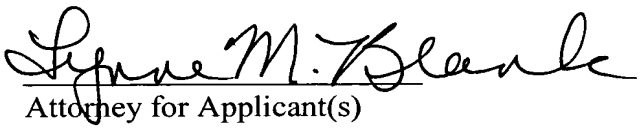
As previously discussed, none of the references teach, suggest or disclose a polymeric particle containing a photographic coupler and a high boiling solvent. As a result, the references fail to teach all the limitations of the present claims.

Table I, pg. 24 indicates that the use of high boiling solvent provides enhanced color formation - as compared to the use of coupler in microspheres alone. Since the undeveloped coupler is loaded in the microsphere, developer must reach the coupler to produce developed coupler, i.e., color. The

presence of high boiling solvent in the microsphere enhances developer penetration, resulting in increased development of the loaded coupler, and enhanced color. T his is a surprising result, based on the teachings found in the prior art.

It is believed that the foregoing is a complete response to the Office Action and that the claims are in condition for allowance. Favorable reconsideration and early passage to issue is therefore earnestly solicited.

Respectfully submitted,



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